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UEX/KSY

In reply to the Written Opinion dated April 19, 2004, we hereby submit an amended claims set.

Thus, the subject-matter as claimed has been limited to the most preferred embodiment of the invention, namely the pharmaceutical compositions for topical administration.

The present invention is based on the finding that voltage-dependent calcium channels are involved in the transduction of mechanical stimulti by nociceptive neurons, so that a corresponding selective antagonist may be used in the topical treatment of peripheral pain.

It should be noted that while the centrally mediated analgenic potential of calcium channel blockers were known, it was hither to not known that such calcium channel blockers may also be effectively used to block mechanoreceptors and, thus, will also be effective in inhibiting pain, when administered topically.

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The subject-matter as claimed is, thus, patentably distinct over the cited prior art.

Dr. Alexa von Uexküll
European Patent Attorney

Enclosure
Amended claims set

AMENDED CLAIMS SET 07. Juni 2004

1. Pharmaceutical composition for the topical administration for the treatment of acute and/or chronic pain comprising calcium channel blockers which are capable of blocking voltage-dependent calcium channels.

2. Pharmaceutical composition as defined in claim 1 wherein the calcium channel is a T-type or L-type channel.

3. Pharmaceutical composition as defined in claim 1 or 2 for the treatment of allodynia or hyperalgesia.

4. Pharmaceutical composition according to any one of claims 1 to 3 wherein the calcium channel blocker is mibefradil, its pharmaceutically acceptable analogues, salts or esters or a dihydropyridine.

5. Pharmaceutical composition for the treatment of pain associated with rheumatoid arthritis, cancer, injuries, back pain, herpes zoster and post-operative pain.

6. Pharmaceutical composition according to any one of claims 1 to 5 for the inhalative or intranasal administration.

7. Pharmaceutical composition according to claim 6 in form of an ointment, gel, crème or a solution or suspension, or plaster.

8. Pharmaceutical composition according to claim 6 in form of a nasal spray or inhalator.

9. Pharmaceutical composition according to any one of claims 1 to 3 characterised in that the drug form used is formed of biologically utilizable or

biodegradable substances wherein the biological materials are proteins or proteides, lipids or lipoids, carbohydrates or polysaccharides or mixtures of several of such materials.

10. Pharmaceutical composition according to any one of claims 1 to 3 characterised in that additionally one other pain killer is used.

11. Pharmaceutical composition according to claim 12 characterised in that the pain killer used in combination is an NSAID, a $5HT_{1D}$ agonist, a dopamin D_2 receptor antagonist, a secale alcaloid, a beta blocker, a calcium channel blocker or a neurokinin antagonist.

12. Pharmaceutical composition according to claim 12 characterised in that the NSAID is ibuprofen, meoxicam, indomethacin or naporxen.

13. Pharmaceutical composition according to claim 12 characterised in that the $5HT_{1D}$ agonist is sumatriptan, MK-452, naratriptan or 311C.

14. Pharmaceutical composition according to claim 12 characterised in that the dopamin D_2 receptor antagonist is metoclopramid.

15. Pharmaceutical composition according to claim 12 characterised in that the secale alcaloid is ergotamin, dihydroergotamin or metergolin.

16. Pharmaceutical composition according to claim 12 characterised in that the beta blocker is propranolol or metoprolol.

17. Pharmaceutical composition according to claim 12 characterised in that the calcium channel blocker is flunarizin or lomerizin.

18. Pharmaceutical composition according to claim 12 characterised in that the pain killer to be administered in combination is acetylsalicylic acid, paracetamol, clonidin, methysergid, dotarizin, lisurid, pizotifen, valproat, aminotraptilin CP-122,288 or UK 116,044.